THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 24

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte ROBERT M. KEENAN

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Appeal No. 95-2851
Application 08/012,379[1]

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ON BRIEF

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Before KIMLIN, WARREN and OWENS, *Administrative Patent Judges*.

OWENS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal from the examiner's refusal to allow claims 1, 2, 4-6, 8-13, 15-17, 19-24, 26-28, 30-33, 67, 68 and 70-99 as amended after final rejection. These are all of the claims remaining in the application.

THE INVENTION

[1] Application for patent filed February 2, 1993.

Appellant's claimed invention is a method for alleviating the tobacco withdrawal syndrome in a human by administering to the human a specified amount of a nicotine metabolite or combination of nicotine metabolites, or their pharmaceutically acceptable salts, and an article for carrying out the method. Claims 1 and 67 are illustrative and read as follows:

1. A therapeutic method to alleviate the tobacco withdrawal syndrome in a human comprising:

administering an amount of a nicotine metabolite or combination of nicotine metabolites or their pharmaceutically acceptable salts thereof to a human in need of such treatment, in an amount in the range of 1 to 100 milligrams per kilogram of body weight of the human per day calculated as the nicotine metabolite or combination of nicotine metabolites in the free base form that is effective to reduce or eliminate symptoms of tobacco withdrawal syndrome.

67. An article of manufacture comprising packaging material and a unit dosage form of a pharmaceutical agent contained within said packaging material, wherein:

said pharmaceutical agent comprises a nicotine metabolite or combination of nicotine metabolites or their pharmaceutically acceptable salts thereof in an amount effective to alleviate tobacco withdrawal syndrome, symptoms of nicotine withdrawal and wherein said packaging material includes instruction means which indicate that said nicotine metabolite or combination of nicotine metabolites or said pharmaceutically acceptable salts thereof can be used by a person in the range of 1 to 100 milligrams per kilogram of body weight of the person per day calculated as the nicotine metabolite or combination of nicotine metabolites in the free base form for alleviating (a) symptoms of tobacco withdrawal syndrome, (b) symptoms of nicotine withdrawal, and (c) the craving associated with the cessation of nicotine use.

THE REFERENCES

References relied upon by the examiner

Hutchinson et al. (Hutchinson)	4,748,181	May 31, 1988
Abood (Abood '162)	4,835,162	May 30, 1989
Bannon et al. (Bannon)	4,946,853	Aug. 7, 1990
Abood (Abood '916)	4,966,916	Oct. 30, 1990

Joseph F. Borzelleca et al., "Studies on the Respiratory and Cardiovascular Effects of (-)-Cotinine", 137 *J. Pharm. Exper. Therapeutics*, 313-18 (1962) (Borzelleca).

References relied upon by the board

Keenan (Keenan '774)	5,573,774	Nov. 12, 1996
Keenan et al. (Keenan '007)	5,596,007	Jan. 21, 1997

THE REJECTION

Claims 1, 2, 4-6, 8-13, 15-17, 19-24, 26-28, 30-33, 67, 68 and 70-99 stand rejected under 35 U.S.C. § 103 as being unpatentable over Abood '916, Abood '162, Bannon, Hutchinson, Borzelleca and appellant's admissions on pages 4-7 of the specification.[2]

OPINION

We have carefully considered all of the arguments advanced by appellant and the examiner and agree with appellant that the aforementioned rejection is not well founded. Accordingly, this rejection will be reversed. We will introduce new grounds of rejection of claims 1, 2, 4-6, 8-13, 15-17, 19-24, 26-28, 30-33, 67, 68 and 70-74 and 91-99 under the provisions of 37 CFR § 1.196(b).

The examiner argues that the Abood references, Bannon and Hutchinson teach

[2] Abood '916 is a division of Abood '162.

that use of nicotine and nicotine agonists and antagonists for the treatment of tobacco withdrawal syndrome was known in the art, and that appellant admits at pages 4-7 of the specification that nicotine was known to metabolize in vivo (answer, page 6). Because nicotine metabolizes in vivo, the examiner argues, administering nicotine by methods including smoking provides an amount of nicotine metabolites which is effective to reduce or eliminate symptoms of tobacco withdrawal syndrome as recited in appellant's claims (answer, pages 8-10). The examiner relies upon Borzelleca for further motivation to use metabolites of nicotine for treating tobacco withdrawal syndrome (answer, page 7). This reference teaches that isolation of nicotine metabolites makes possible the investigation of the role of metabolites of nicotine in controlling or limiting the response to nicotine (page 313). Borzelleca discloses that in a reported preliminary study of anesthetized dogs, several nicotine metabolites produced depression, and high dosages produced death (page 314). Borzelleca reports that in his studies, (-)-cotinine produced depression in most mice and hyperexcitability in a few (page 316). We find in this reference no indication that nicotine metabolites are effective for reducing or eliminating the symptoms of tobacco withdrawal syndrome.

The examiner's argument is not well taken because the examiner has provided no evidence or convincing reasoning which shows that the amount of cotinine produced by metabolism of nicotine ingested during smoking is within the range recited in

appellant's claims and is sufficient to reduce or eliminate symptoms of tobacco withdrawal syndrome. The Benowitz article[3] cited in appellant's specification (page 8) teaches that cotinine is the major metabolite of nicotine and is present in the blood of tobacco smokers in much higher concentrations and remains longer than nicotine after cessation of smoking (page 604). Benowitz infused the fumarate salt of cotinine into subjects at a rate of 4 Fg base/kg/min for 60 min (page 605). This amount "was selected as one which would induce blood concentrations of cotinine in the range of that achieved by moderately heavy cigarette smokers" (page 605). Benowitz states that the cotinine infusion produced a significant reduction in the desire to smoke (page 607) but also states that this reduction "was of a magnitude consistent with the expected reduction in preexperimental anxiety and tension that we usually see with similar subjects and paradigms that also include placebo infusions" (page 610). Benowitz concludes that "at levels to which smokers are generally exposed, cotinine exerts little, if any, pharmacologic effect" (page 610).

The amount of cotinine infused by Benowitz, i.e., 4 Fg/kg/min for 60 min, which, Benowitz states, is an amount which would induce blood concentrations of cotinine in the range of that achieved by moderately heavy cigarette smokers (page 605), is 240 Fg/kg, which is less than one fourth the minimum amount of nicotine metabolite recited

[3] Neal L. Benowitz et al., "Cotinine disposition and effects", 34 *Clin. Pharmacol. Ther.* 604-11 (1983).

in appellant's claims, and Benowitz concludes that the infused amount has little if any pharmacologic effect (page 610). This reference, therefore, indicates that the amount of cotinine which is in the bloodstream of a moderately heavy cigarette smoker would not have the pharmacologic effect of reducing or eliminating symptoms of tobacco withdrawal syndrome.

Furthermore, Bannon teaches that as nicotine levels fall after smoking, additional nicotine is required to suppress the urge to smoke (col. 1, lines 53-68).

The examiner does not point out, and we do not find in the references relied upon by the examiner, any indication that the total nicotine metabolites produced by smoking would build up in the blood stream in an amount which is within the range recited in appellant's claims and which would be effective for reducing or eliminating symptoms of tobacco withdrawal syndrome as required by these claims.

For the above reasons, we conclude that the examiner has not carried her burden of establishing a *prima facie* case of obviousness of appellant's claimed invention.

Under the provisions of 37 CFR § 1.196(b), we enter the following new grounds of rejection.

Claims 1, 2, 4-6, 8-13, 15-17, 19-24, 26-28, 30-33, 67, 68, 70-74 and 91-99 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-26 of Keenan '007 in view of appellant's admitted prior art, and claims 67, 68

and 70-74 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-17 of Keenan '774 in view of appellant's admitted prior art.[4]

Claims 13 and 26 of Keenan '007 differ from appellant's independent method claims 1, 12, 23 and 91 in that the Keenan '007 claims recite administering cotinine or a pharmaceutical salt thereof,[5] whereas appellant's claims 1, 12, 23 and 91 recite administering a nicotine metabolite or combination of nicotine metabolites or pharmaceutical salts thereof. Appellant's dependent claims 2, 13, 24 and 92 recite that the nicotine metabolite can be, *inter alia*, (-)-cotinine. The teaching by Keenan '007 of use of cotinine would have fairly suggested, to one of ordinary skill in the art, use of a nicotine metabolite because, as acknowledged by appellant (specification, page 4), cotinine was a known nicotine metabolite. Use of the methods of administering the nicotine metabolite recited in appellant's claims which depend from claims 1, 12, 23 and 91 would have been *prima facie* obvious to one of ordinary skill in the art in view of the recitation of such methods in the dependent claims of Keenan '007.

Regarding appellant's article claims 67, 68 and 70-74, given that cotinine is administered as recited in the Keenan '007 claims, it would have been apparent to one

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[4] No rejection is applied to claims 75-90.

[5] Keenan '007 at col. 6, lines 11-17 indicates that the amount of cotinine which, as recited in the Keenan '007 claims 13 and 26, is the same as the amount recited in appellant's independent claims, is calculated as (-)-cotinine in the free base form.

of ordinary skill in the art that an article which contains the appropriate amount of cotinine and instructions for administering it would be needed to carry out the method.

Appellant's claims 67, 68 and 70-74 differ from the Keenan '774 claims in that appellant's claims recite that the article contains a means for instructing that the contents can be used in an amount of 1 to 100 mg/kg of body weight to alleviate the symptoms of tobacco withdrawal, nicotine withdrawal, and craving associated with the cessation of nicotine use. Given that the Keenan '774 article is for use by a human to suppress appetite, prevent weight gain or induce weight loss as recited in the Keenan '774 independent claims, it would have been *prima facie* obvious to one of ordinary skill in the art to include instructions as to how to administer the contents of the article for that purpose. The instructions would differ from those recited in appellant's claims only in the wording of the instructions. Because the printed matter in the instructions has no functional relation with the substrate on which it appears, it does not distinguish appellant's claimed invention over that of Keenan '774. *See In re Gulack*, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983). Hence, the article recited in appellant's claims 67, 68 and 70-74 would have been *prima facie* obvious to one of ordinary skill in the art over claims 1-17 of Keenan '774.

DECISION

The rejection of claims 1, 2, 4-6, 8-13, 15-17, 19-24, 26-28, 30-33, 67, 68 and 70-99 under 35 U.S.C. § 103 over Abood '916, Abood '162, Bannon, Hutchinson,

Borzelleca and appellant's admissions on pages 4-7 of the specification is reversed. New grounds of rejection of claims 1, 2, 4-6, 8-13, 15-17, 19-24, 26-28, 30-33, 67, 68, 70-74 and 91-99 have been entered under 35 U.S.C. § 1.196(b).

This decision contains in a new ground of rejection pursuant to 37 CFR § 1.196(b) (amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53,131, 53,197 (Oct. 10, 1997), 1203 Off. Gaz. Pat. & Trademark Office 63,122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides that "[a] new ground of rejection shall not be considered final for purposes of judicial review."

37 CFR § 1.196(b) also provides that the appellant, WITHIN TWO MONTH FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection of avoid termination of proceedings (37 CFR § 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner . . . .
>
> (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record . . . .

No time period for taking subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED, 37 CFR § 1.196(b)

EDWARD C. KIMLIN Administrative Patent Judge	)
CHARLES F. WARREN Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
TERRY J. OWENS Administrative Patent Judge	)

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